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Review Article

Oral Cancer – Risk Factors, Staging and Treatment: A Review

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Abstract:
The sixth-most common malignancy in the world was oral cancer. The most common risk factors for developing oral cancer are tobacco, smoking, alcohol, and HPV infection. Most malignant oral tumours are detected at an advanced stage. AJCC staging of tumours gives better treatment for malignancies. Surgery is the first-line treatment, followed by radiotherapy and chemotherapy for patients who are not able to tolerate surgery. In this paper overview the various risk factors, staging, and treatment of oral cancer have been reviewed.
Key words: Malignancy, AJCC staging, Radiotherapy, Chemotherapy

Introduction

A malignant neoplasm that develops on the lip or oral cavity is called oral cancer[1]. The floor of the mouth, gingiva, anterior tongue, check and any other portion of the oral cavity might be affected by oral cancer. The 6th most recurrent malignancy worldwide is oral cancer; India, oral cancer has greatest incidence of any malignancy, accounting for between 50-70% of all cancer related deaths[2]. Males are most commonly affected with oral cancer compared to females[3]. Most oral cancers exhibit a lack of initial signs and symptoms and predicting patients with oral malignancy has remained refined[4].

Risk factors

Tobacco

90% of male oral cancer mortality occurs due to the consumption of tobacco. Oral cancer has been linked to the consumption of all tobacco products, including cigarettes, chewing tobacco, cigars and smokeless tobacco[4].The aromatic hydrocarbon Benz- pyrene and tobacco specific nitrosamines [TSNS] specifically, 4-[nitroso methylamino]-1-(3-pyridyl)-1-butanone [NNK] and N-nitrosonornicotind [NNN] are the two main cancer - causing substances in tobacco. NNK and NNN metabolites bind to the keratinocyte stem cells of DNA and generate DNA adduct. These DNA adducts are involved in mutation[5].

Alcohol

Alcohol consumption is another important risk factor for the occurrence of oral cancer[4]. Alcohol is metabolized into acetaldehyde by the enzyme alcohol dehydrogenase. Acetaldehyde may interpretate to the DNA synthesis and cause

DNA damage[5]. Acetaldehyde was a highly toxic carcinogen and chronic alcohol consumption promotes tumors of oral cancer[6].

Betel quid

Betel leaf, areca nut, slaked lime and tobacco are the most frequent incorporate of betel quid. Betel quid contains are shows genotoxic cytotoxic and cell stimulate cell proliferation conducted study in invitro studies on oral mucosal fibroblasts assays by using DNA damage, cytotoxicity and cell proliferation[5]

Diet and nutrition

Higher consumption of fruits and vegetables including carrots, tomatoes and green peppers was associated with a lower risk of mouth and throat cancer. some food groups are at increased risk for oral cancer, including nutritional deficiencies, particularly in processed meat, cake and desserts, butter, eggs, soups, cheese, pasta, bread, corn etc. have been associated with a higher risk of oral cancer[5].

Mouth wash

Oral cancer has also been linked to the usage of mouthwash[4]. Alcohol is typically used in mouthwash as a solvent for additional components or a preservative[5]. Ethyl alcohol, which is present in mouthwash, has not been linked to oral cancer due to a lack of sufficient clinical data[4]

Occupational risk

Solar exposure is another factor that significantly threatens lip cancer. Compared to women, men have three times more exposure to lip cancer due to their occupation, smoking and sun radiation[4]. Actinic cheilitis, which may progress into a carcinogen, is also caused by UV rays. Most common carcinogenic chemicals like sulfur dioxide, asbestos, pesticides, exposure and mists from strong inorganic acids and fossil flues burning cause mouth, larynx and pharynx cancer. Production of rubber products, plumbing [exposed to metals] and woodworking in automobile industry are the main carcinogen-causing occupations[5].

Dental factors

Oral unhygienic and dental infections are probable to develop chronic ulceration and promote neoplasma due to the carcinogenic activity of tobacco[2,5].

Genetic factor

Patient with head and neck cancer have a higher risk of developing it due to abnormal chromosome mutation[4]. OSCC [oral squamous cell carcinoma], particularly tongue and buccal mucosal cancer, is greatly influenced by genetic predisposition. Some researchers believe that people who have inherited the inability to metabolize cancer-causing substance that have the potential to cause cancer are unable to repair DNA damage and are therefore susceptible to developing an oral malignancy[6].

Viral infection

HIV [human immunodeficiency virus] and HPV [human papillomavirus] viruses are primarily responsible for the advancement of oral cancer[6]. These viral genes and their products can affect cell growth and multiplication; some viral genes are proto-oncogenes that convert into oncogenes when they are introduced into the host's DNA, leading to malignant transformation. HHV [human herpesviruses], HPV and ASV [avian sarcoma virus] are the archetype viruses connected to the emergence of oral cancer. In immunosuppressed patient EBV [Epstein-Barr virus] develops oral hairy leukoplakia and lymphoproliferative disease. Condyloma acuminatum, verruca vulgaris and focal epithelial hyperplasia [heck's disease] and benign proliferative lesions like papilloma's are all caused by HPV. E_6 and E_7 are the two major oncoproteins encodes HPV[5]. E_6 protein enhance the breakdown of P_{53} tumor suppress protein expression. E_7, which reassure the disruption of pRb, a result of the tumor suppressor gene[1]. Which results in disruption of cell cycle, abnormal DNA replication, DNA repair and apoptosis[5].

Fungal infection

Candida albicans species was the most common causative organism for fungal infection, occurred by superficial fungal hyphae of candida albicans result in leukoplakia particularly nodular leukoplakia leads to malignant transformation by oral premalignant lesions. Candida species were present in the oral cavity and may have caused host Immunosuppression to pathological condition or treatment[5]. Dysplasia and malignant transformation were the primary incidence of candid[2].

Staging of tumor

In 1968, UICC [International Union against Cancer] first published TNM staging, followed by AJCC [American Joint Committee on Cancer] in 1977, which published a staging manual for cancer, whereas in 2017 the 8th version of UICC and AJCC TNM staging was released. The TNM classification includes the size of the primary tumor [T], involvement of locoregional Lympnodes [N] and distant metastasis [m][7]. In 8th edition contains the variables like depth of invasion [DOI] and extra nodal extension [ENE] to the pT and pN, which are used to measure tumor size[8]. The pT1 stage of tumor of 2cm or less in greatest dimension and 5mm or less of DOI, pT3stage tumor was greater than 2cm to 4 cm in dimension and DOI less than 10mm, in pT3 stage tumor was greater than 4cm and DOI more than 10 mm. If a single node with a diameter of less than 3cm is present, ENE is staged as pN2a, and the stage for other patients is pN3b[9]. TNM classification was useful for therapy planning, risk estimation, and assessment of quality of life[7].

Management

In the late stage of oral cancer, the tumour is large and spread to the lymph nodes; nearly two-third of patients is diagnosed. This condition requires more intensive management, which increases the risk of mortality and morbidity and lowers the quality of life. Surgery, radiotherapy and chemotherapy are the main treatment used for oral cancer. In the early stage [stage l and ll], monotherapy was used, whereas in the advances stage [stage lll and lV] combination treatment is used[10].

Surgery and neck dissection

Surgery is the first- line treatment for oral cancer. For intensive- stage surgery, along with radiotherapy and /or chemotherapy[10]. In early-stage oral cancer [stage l and ll], surgery was offered with no lymph node spread [N_o] and no evidence of metastasis [M_O] in areas of decreased risk for metastasis[11]. It depends upon the number, size and site of the lymph nodes at the level at which neck dissection was carried out[10].

Radiotherapy

Radiation therapy generally aims to damage DNA, multiplying cancer cells in a localized area while protecting surrounding tissue and function[10]. Early stages of tumours are treated with radical radiotherapy, whereas advance stages of radiotherapy combine chemotherapy or targeted therapy with monoclonal antibiotics that act against epidermal growth factor receptor [EGFR] to make the radiations cytotoxic effects more potent[12]. External beam radiation and brachytherapy are the two main types of radiotherapy. Brachytherapy is an internal radiation treatment that involves the surgical placement of a radioactive insert into the tumour to treat the tumour[10]. External beam radiation increases the total dose in two ways; a) by a rise in the total dose with hyperfractionation; b) by decreasing the duration of accelerated fractionation radiotherapy[12]. External beam radiation is more common for head and neck cancer treatment using a linear accelerator that concentrates radiation on the tumour location. Daily outpatient external beam radiotherapy is given over the course of around 6 weeks[10]. The dose of radiation varied, but approximately 60 Grey [GY] were split into 30 daily fractions of 2GY for each cycle of 6 weeks[11].

Chemotherapy

For oral cancer, chemotherapy is used as a palliative treatment. The main aim was to destroy multiplying abnormal cancer cells in order to manage the spread and metastasis of tumour[10]. Chemotherapy and immunotherapy are known as systemic therapies, which are for treatment[13]. Chemotherapy is mainly split into three groups; induction chemotherapy means before surgery. It is mainly used in advanced stage with lymph nodal involvement and also increases the risk of recurrence of tumor and metastases[10]. Adjuvant chemotherapy is used after surgery to reduce the incidence of recurrence of metastasis[13]. Concurrent chemotherapy is used in conjunction with radiation treatment. The general class of chemotherapeutic agents like cisplatin and carboplatin are platinum compounds; methotrexate and 5-fluoro uracil are antimetabolitesclass; docetaxel are taxanes; plant alkaloids, hydroxyurea, anthracycline and taxoids. Induction therapy shows efficacy with the combination of 5- fluorouracil, docetaxel and cisplatin. Target therapy agents like cetuximab, a monoclonal antibody that target the epidermal growth factor [EGFR][10]. In metastatic disease, cisplatin or carboplatin are the front-line treatment combination chemotherapy agents like 5-fluorouracil, docetaxel and paclitaxel[13]. During or after treatment of cancer most common adverse toxic effects are xeroderma, mucositis, alopecia, sever nausea and vomiting, neurotoxicity, weight loss, stomatitis, nephrotoxicity and ototoxicity[11].

Conclusion

Oral cancer was most common in males due to risk factors like smoking, alcohol, tobacco, and occupational exposure. Due to the increased morbidity and mortality rates, a more effective treatment plan is needed for oral cancer. Public and clinical awareness are required to improve quality of life because most malignancies are not detected at an early stage. Advance treatment was required to improve the disease condition or recurrence and the quality of life of the patient.

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